Having already approved two biosimilar agents for use in the US—including Inflectra, a biosimilar to Janssen Biotech, Inc.’s Remicade (infliximab) for psoriasis and psoriatic arthritis among other indications—the FDA is currently collecting public comments on its draft guidance for industry on biosimilar labeling. “Labeling for Biosimilar Products,” published in March, has earned praise from some corners while generating concern from others. The comment period closes next month.

THE DATA GAME

A major sticking point for some detractors is the suggestion that most biosimilar labels will not require a description of data from clinical studies designed to demonstrate biosimilarity (Section III). FDA believes such information, “would not be useful for health care practitioners,” the guidance states.

Among those concerned about this assertion is Biotechnology Innovation Organization (BIO). In its comments to the FDA, BIO said the “approach to labeling appears to be grounded in the notion that providing clear and complete information about a biosimilar product is unnecessary and would somehow be misinterpreted by educated prescribers.”

The comment continues, “As BIO has long advocated, the labeling for a biosimilar should flow from the fundamental premise that due to the scientific complexities of biologics, biosimilars are neither expected nor required to be structurally identical to the reference product. In this regard, more information is preferable to less.”

Leah Christl, PhD, Associate Director for Therapeutic Biologics and lead of the FDA’s Therapeutic Biologics and Biosimilars Staff in the Office of New Drugs noted in a blog posting about the draft guidance that comparative data generally will be available to the public on the Drugs@FDA website. Dr. Christl observed in her post, “The goal of a biosimilar development program is to demonstrate biosimilarity between the proposed product and the reference product, not to independently establish the safety and effectiveness of the proposed product.”

In a statement to Practical Dermatology®, the Biologics Prescribers Collaborative (BPC) asserted that, “As biologic prescribers, we appreciate FDA highlighting the distinctions between the labeling needs of a biosimilar and a generic drug, especially by adding in a statement of biosimilarity. However, to promote transparency and uphold patient safety, the final guidance should include a statement on the interchangeability status of the biosimilar and provide either a summary or link of the full clinical data submitted in support of the biosimilar approval.”

Jashin J. Wu, MD, Co-chair of the IPC Biosimilars Working Group, says clinical trial data should be included in the prescribing information, “as transparency is imperative to physicians.” Speaking from his personal perspective and not on behalf of the IPC, he added, “Due to the complex folding of these molecules, biosimilars are not exactly the same as the originator, so there may be slight variation in the efficacy and safety as well.”

FDA proposes that biosimilar product labeling be required to comply with the content and format requirements of the pregnancy and lactation labeling final rule (“PLLR”), even if the reference product was not required to do so. That guidance has drawn concern from the Biosimilars Forum, which questioned the feasibility of compliance, “because the biosimilar manufacturer does not have access to the reference product data (i.e., clinical and non-clinical post-marketing data of product use during pregnancy and lactation).”

For some skeptics of biosimilars, these issues underscore a more general concern—namely that biologic agents may not be “similar” to a reference drug in the sense that a small molecule generic is “similar” to its reference.

As Andrew Blauvelt, MD, MBA, President of Oregon Medical Research Center, explains “Biosimilars are technically not generic medications, because they are not chemically identical to originator drugs. However, they are essentially highly similar to original biologics. In fact, for them to be approved by the FDA, biosimilars undergo extensive side-by-side comparisons with originator biologics in hundreds of different laboratory and clinical studies. For them to be
approved, biosimilars can perform no better and no worse than the original biologics that they resemble. In this manner, the FDA has cut the cost of developing biosimilars to around 20 percent of the cost of developing an original biologic.”

The lower cost of biosimilars may increase access to therapy, Dr. Blauvelt says. Former Chair of the Biosimilar Working Group of the IPC, Dr. Blauvelt notes that no long-term efficacy and safety studies are performed prior to FDA approval of biosimilars, but he does not anticipate long-term problems. “Unforeseen problems, in my opinion, would not be expected to develop over time, given the high degree of biosimilar chemical and structural similarity to original biologics, where long-term performance in clinical studies is well established,” he says.

WHAT’S IN A NAME?

The Biosimilars Forum voices concern about draft guidance on use of biosimilar, reference, and core names within labeling, stating that, “FDA’s suggestions…are indefinite and could lead to uncertainty and inconsistent labeling.” They note the proposed use of the reference product name may cause trademark or other intellectual property issues. The group urges that FDA adopt a “meaningful suffix” rather than a randomly generated modifier, when devising drug names.

The BPC has also called on the FDA to rethink its use of random modifiers, stating on its website that meaningful suffixes, “would be more memorable, limit confusion, and hold manufacturers accountable.” They point to FDA’s initial naming convention for Sandoz’s biosimilar of filgrastim, marketed as Zarfio: filgrastim-sndz. The new proposed name is filgrastim-bflm.

The IPC also urges the establishment of meaningful product names. “Until then,” the group recommends that, “biosimilars and originator biologics should not be randomly interchanged, since it would be impossible to accurately assess loss of efficacy and adjudicate adverse effects in the setting where drug switching may occur haphazardly at the pharmacy level.”

As CMS continues to refine policies for billing and reimbursement of biosimilars, naming conventions could take on additional significance. According to Esther Scherb and Kassie Maldonado of Covington & Burling LLP, CMS revised the billing code for Neupogen (filgrastim) in June, to exclude biosimilars. HCPCS code Q5101 has been designated for the biosimilar. CMS is also requiring the use of mandatory modifiers to identify the manufacturer of any administered biosimilar (see www.cov.com.) Meaningful suffixes could eliminate the need for such billing modifiers.

As with so much in healthcare today, the reimbursement determinations may rule the day. “In the end,” Dr. Wu predicts, “physicians may not have much of a say in the matter of prescribing an originator vs. a biosimilar; the health insurance will likely have the final say in terms of limiting choices or approving certain products.”